Oncology Clinical Pathways
Prostate Cancer

April 2022 – V3.2022

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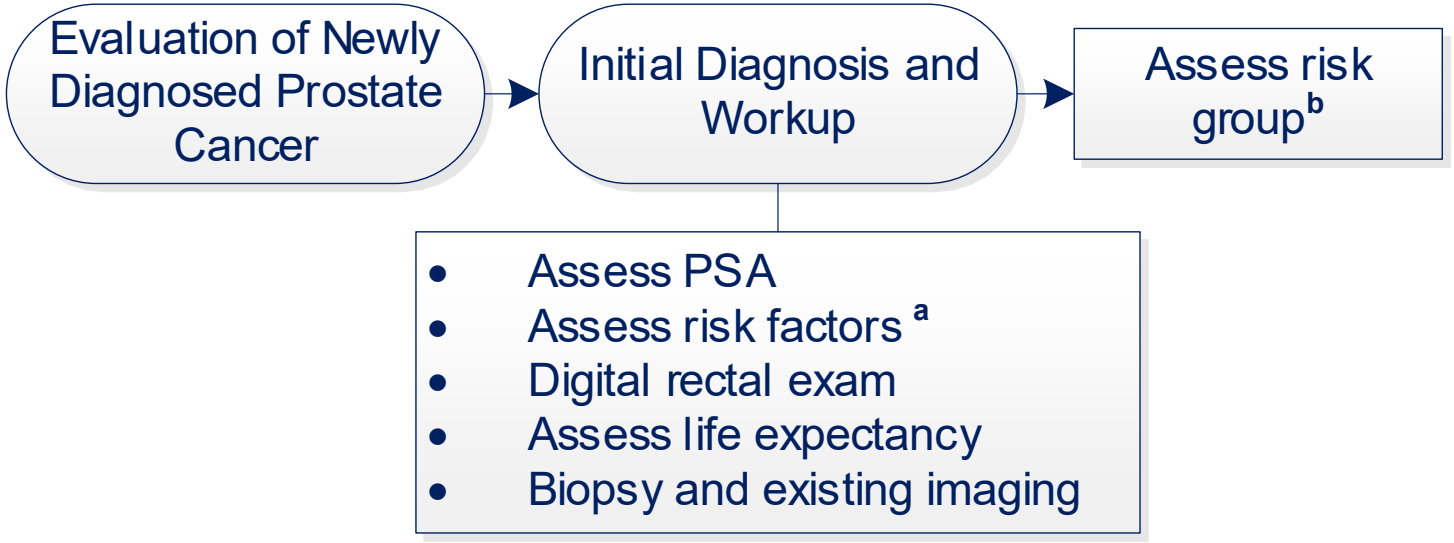
Prostate Cancer – Evaluation of Newly Diagnosed



Clinical trial(s) always considered on pathway.

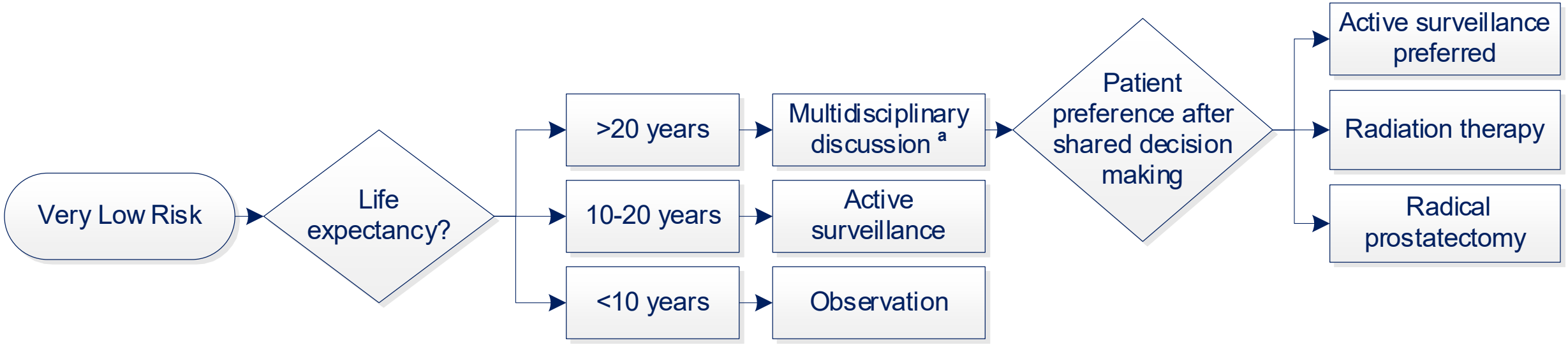
[a] **Risk Factors** Race, Agent Orange exposure, family history, known germline mutation

[b] **Risk Groups** Refer to risk stratification and corresponding pathways

Prostate Cancer – Risk Stratification

Risk Group	Defined by Clinical/ Pathologic Features			Imaging for Nodal or Metastatic Disease	Germline Testing	Initial Therapy
Very low	All the following: • T1c • Grade group 1 • PSA < 10 ng/ml • < 3 prostate biopsy fragments/ cores positive; ≤ 50% cancer in each fragment/core • PSA density < 0.15 ng/ml/g			Not indicated	Recommended for any of the following: • Ashkenazi Jewish ancestry • Family history of high-risk germline mutations • Strong family history of cancer	Follow **Very Low Risk** pathway
Low	All the following: • T1-T2a • Grade Group 1 • PSA < 10 ng/ml					Follow **Low Risk** pathway
Intermediate	All the following: • No high-risk group features • No very high-risk group features • One or more intermediate risk factors (IRF) ○ T2b-T2c ○ Grade Group 2 or 3 ○ PSA 10-20 ng/ml	***Favorable Intermediate***	All the following: • One IRF • Grade Group 1 or 2 • < 50% positive biopsy cores	• Bone imaging not recommended for staging • Pelvic ± abdominal imaging recommended if nomogram predicts >10% probability of pelvic LN involvement		Follow **Favorable Intermediate Risk** pathway
		Unfavorable Intermediate	At least one of the following: • 2 or 3 IRFs • Grade Group 3 • ≥ 50% positive biopsy cores	• Bone and Soft Tissue Imaging: use PSMA PET/CT, (or PET/MRI) if available, or a combination of bone imaging (with either Tc99m-MDP/HDP SPECT/CT, F18-NAF PET/CT) + soft tissue imaging (with CT, MRI, F18-fluciclovine PET) + PSMA PET/CT for equivocal findings • Consider molecular imaging if available		Follow **Unfavorable Intermediate Risk** pathway
High	At least one high-risk feature: • T3a • Grade Group 4 or 5 • PSA > 20 ng/ml			• Bone and Soft Tissue Imaging: use PSMA PET/CT, (or PET/MRI) if available, or a combination of bone imaging (with either Tc99m-MDP/HDP SPECT/CT, F18-NAF PET/CT) + soft tissue imaging (with CT, MRI, F18-fluciclovine PET) + PSMA PET/CT for equivocal findings • Consider molecular imaging if available	Recommended	Follow **High or Very High-Risk** pathway
Very High	At least one of the following: • T3b-T4 • Primary Gleason pattern 5 • 2 or 3 high-risk features • > 4 cores with Grade Group 4 or 5			• Bone and Soft Tissue Imaging: use PSMA PET/CT, (or PET/MRI) if available, or a combination of bone imaging (with either Tc99m-MDP/HDP SPECT/CT, F18-NAF PET/CT) + soft tissue imaging (with CT, MRI, F18-fluciclovine PET) + PSMA PET/CT for equivocal findings • Consider molecular imaging if available	Recommended	
Regional	Any T, N1, M0: Consider testing tumor for HRRm and MSI or dMMR				Recommended	Follow **Regional Risk** pathway
Metastatic	Any T, Any N, M1: Recommend testing tumor for HRRm and MSI or dMMR				Recommended	Follow **CSPC M1** pathway

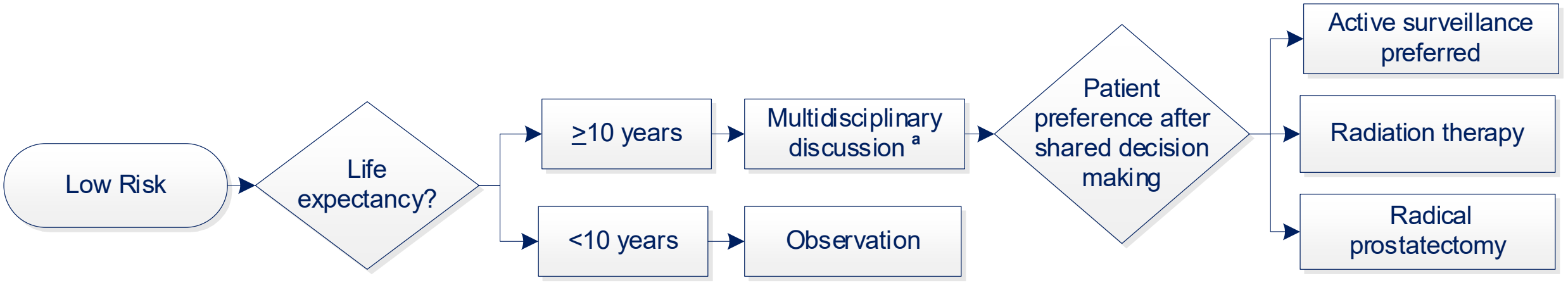
Prostate Cancer – Very Low Risk Group



Clinical trial(s) always considered on pathway.

[a] **Multidisciplinary discussion** to include Radiation Oncology, Urology

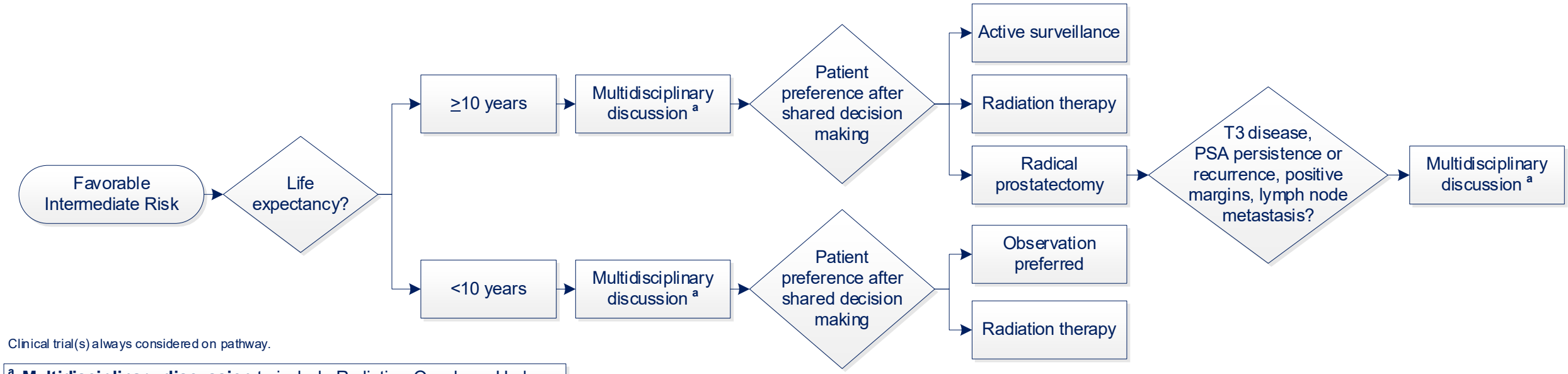
Prostate Cancer – Low Risk Group



Clinical trial(s) always considered on pathway.

[a] **Multidisciplinary discussion** to include Radiation Oncology, Urology

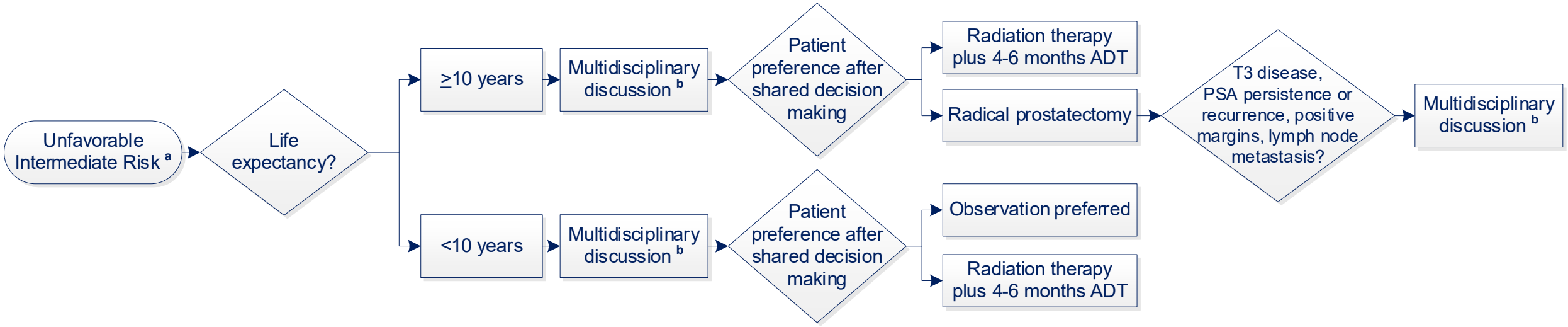
Prostate Cancer – Favorable Intermediate Risk Group



Clinical trial(s) always considered on pathway.

[a] **Multidisciplinary discussion** to include Radiation Oncology, Urology

Prostate Cancer – Unfavorable Intermediate Risk Group

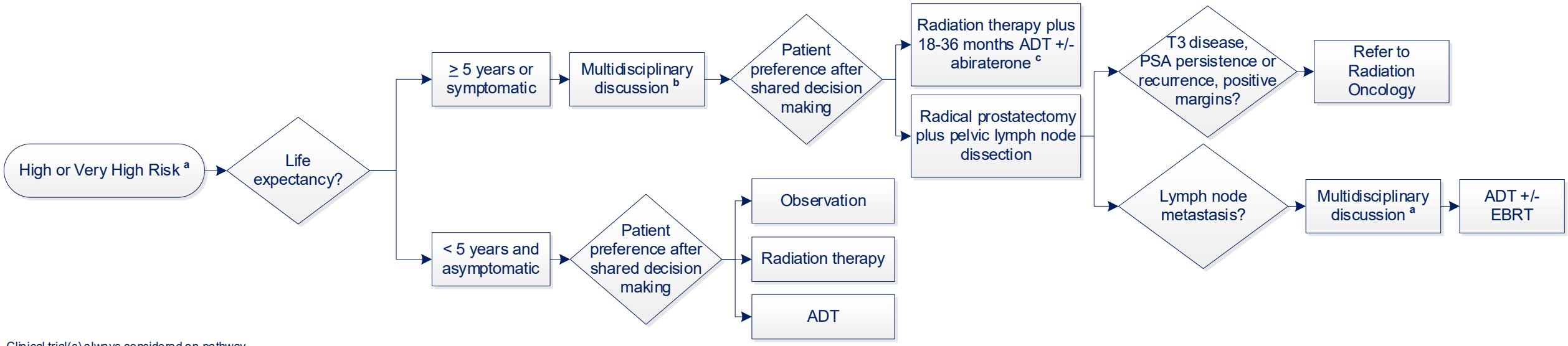


Clinical trial(s) always considered on pathway.

[a] **Imaging** PSMA PET/CT, (or PET/MRI) if available, or a combination of bone imaging (with either Tc99m-MDP/HDP SPECT/CT, F18-NAF PET/CT) + soft tissue imaging (with CT, MRI, F18-fluciclovine PET) + PSMA PET/CT for equivocal findings

[b] **Multidisciplinary discussion** to include Radiation Oncology, Urology, Medical Oncology

Prostate Cancer – High or Very High Risk Group



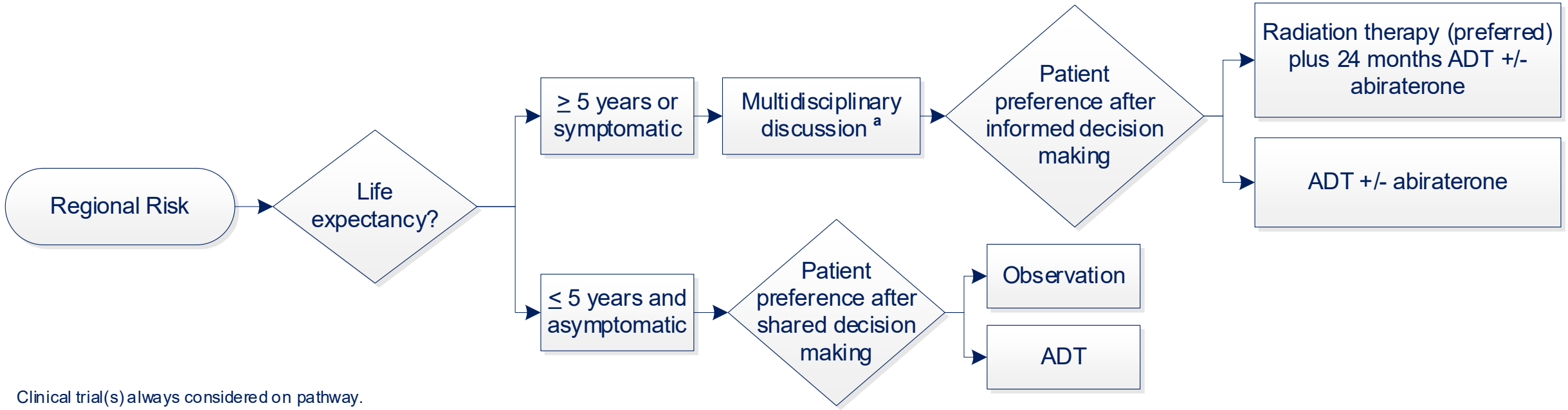
Clinical trial(s) always considered on pathway.

[a] **Imaging** PSMA PET/CT, (or PET/MRI) if available, or a combination of bone imaging (with either Tc99m-MDP/HDP SPECT/CT, F18-NAF PET/CT) + soft tissue imaging (with CT, MRI, F18-fluciclovine PET) + PSMA PET/CT for equivocal findings

[b] **Multidisciplinary discussion** to include Radiation Oncology, Urology, Medical Oncology

[c] **Prescribe abiraterone** only for very high risk group patients; duration for maximum of 2 years

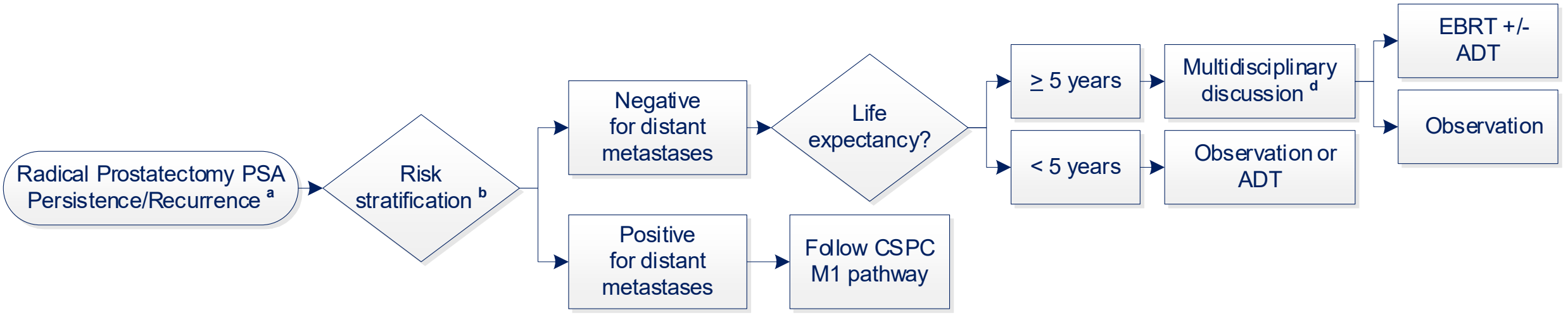
Prostate Cancer – Regional Risk Group



Clinical trial(s) always considered on pathway.

[a] **Multidisciplinary discussion** to include Radiation Oncology, Urology, Medical Oncology

Prostate Cancer – Radical Prostatectomy PSA Persistence/Recurrence



Clinical trial(s) always considered on pathway.

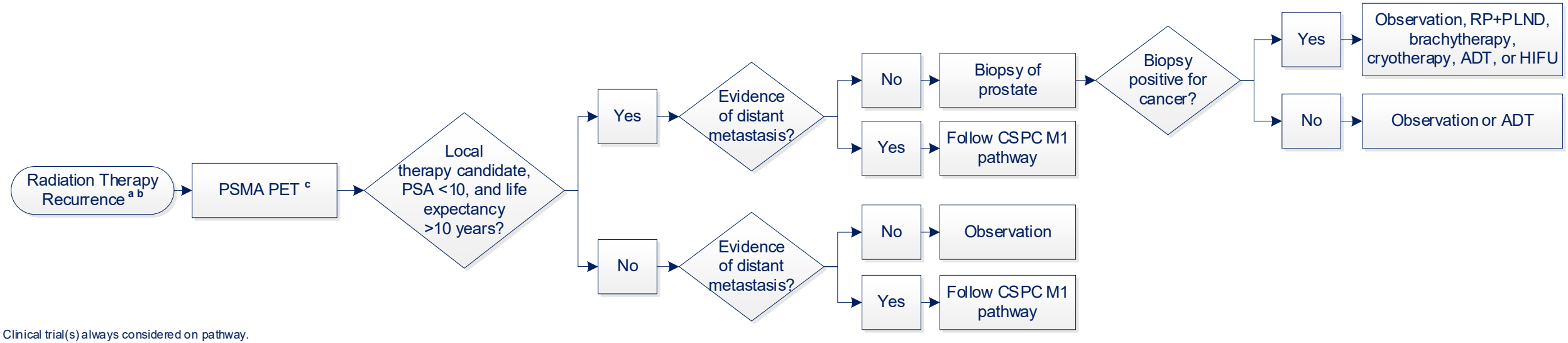
[a] **PSA Persistence/Recurrence** defined as rising, detectable PSA based on at least two determinations

[b] **Risk Stratification** PSADT; pathology report: PSMA PET imaging, if not available: fluciclovine PET/CT; CT chest/abdomen/pelvis; bone imaging with Tc99m-MDP/HDP SPECT/CT or F18 sodium fluoride PET/CT (or PET/MRI); MRI prostate/pelvis; provider appropriateness review and consideration should be made for imaging evaluation in the setting of early recurrence with low PSA values (<0.5 ng/ml)

[c] **Multidisciplinary discussion** to include Radiation Oncology, Urology, Medical Oncology

EBRT: External Beam Radiation Therapy

Prostate Cancer – Radiation Therapy Recurrence



Clinical trial(s) always considered on pathway.

[a] **Recurrence** defined as rising PSA >2 above Nadir or positive DRE post-curative intent radiation

[b] **PSA Bounce** defined as a transient rise in PSA, at a median of 12-18 months after treatment; PSA bounce may occur in the absence of recurrent disease and does not necessarily signify a treatment failure or constitute an indication for intervention

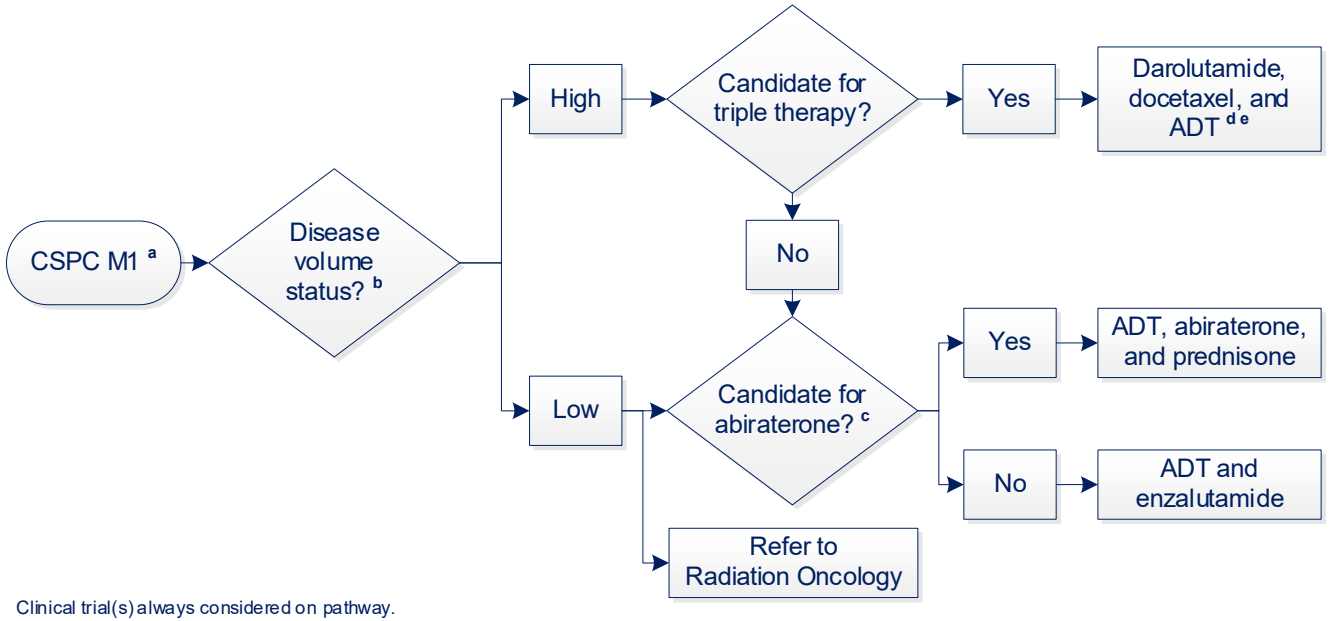
[c] **If PSMA PET imaging is not available**, recommend prostate MRI and fluciclovine PET/CT or CT chest/abdomen/pelvis and bone imaging (technetium bone scan or F-18 sodium fluoride PET)

RP: Radical Prostatectomy

PLND: Pelvic Lymph Node Dissection

HIFU: High Intensity Focused Ultrasound

Prostate Cancer – Castrate Sensitive Prostate Cancer (CSPC) M1



Clinical trial(s) always considered on pathway.

[a] **First generation antiandrogens** are not recommended for long-term use however short course may be administered to block testosterone flare

[b] **Low-volume disease** defined as no visceral metastases and four or less bone metastases; **high volume disease** is differentiated from low-volume disease by visceral metastases and/or more than four bone metastases

[c] **Abiraterone** contraindications include hepatic dysfunction [f], significant cardiovascular disease [g], uncontrolled hypertension, or the inability to tolerate prednisone

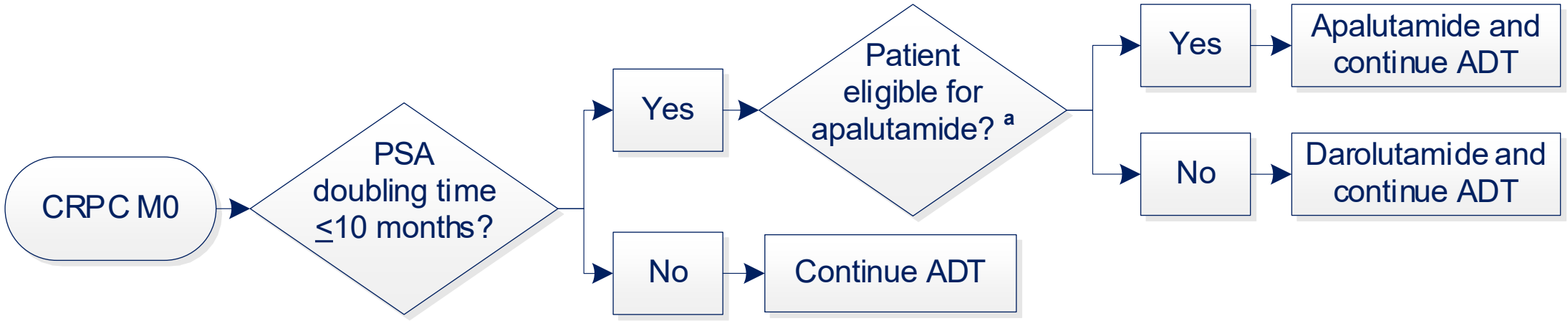
[d] **Inclusion Criteria** includes ECOG 0-1 and distant metastasis (M1) detected on imaging

[e] **Exclusion Criteria** includes CVA, MI, unstable angina, CHF (NYHA class III or IV) in the prior 6 months and/or uncontrolled HTN

[f] **Hepatic dysfunction** defined as baseline Tbili ≥ 1.5 x ULN (except in Gilbert's Disease), AST or ALT ≥ 2.5 x ULN (AST or ALT ≤ 5x ULN allowed in known liver metastases), and/or Child-Pugh Class C

[g] **Significant CV disease** defined as MI or ATE in past 6 months, severe or unstable angina, NYHA Class III or IV heart failure, and/or EF < 50% at baseline

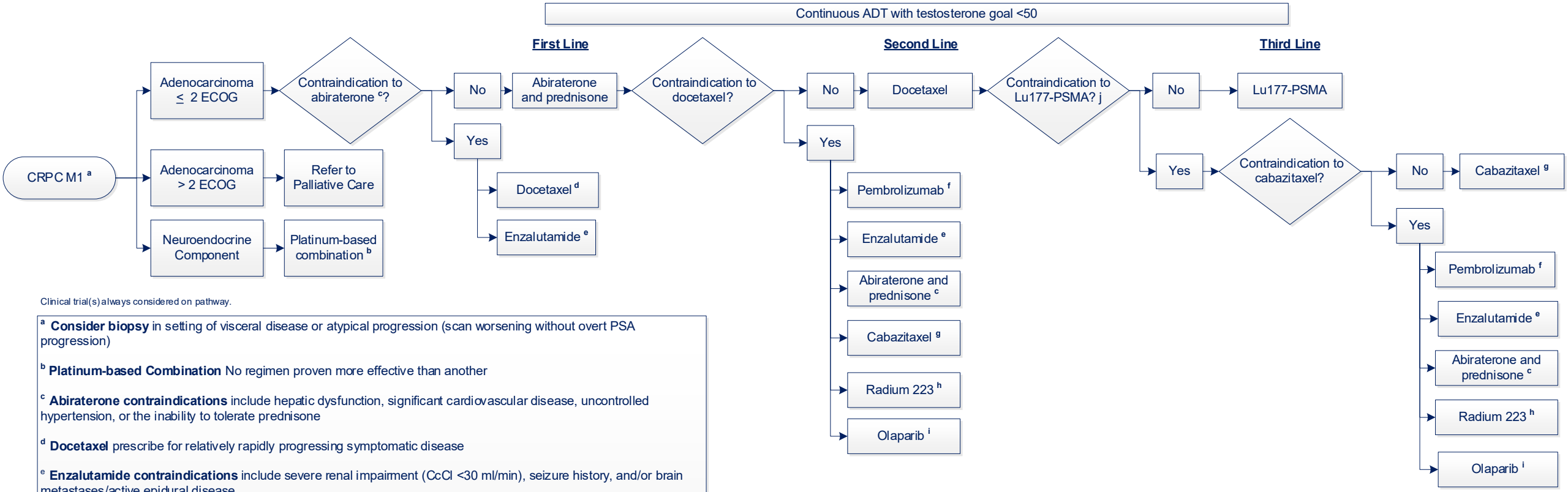
Prostate Cancer – Castrate Resistant Prostate Cancer (CRPC) M0



Clinical trial(s) always considered on pathway.

[a] **Apalutamide** contraindications include history of severe renal or hepatic dysfunction, cardiovascular or cerebrovascular event in prior 6 months, high fall risk, or seizure history

Prostate Cancer – Castrate Resistant Prostate Cancer (CRPC) M1



Clinical trial(s) always considered on pathway.

[a] **Consider biopsy** in setting of visceral disease or atypical progression (scan worsening without overt PSA progression)

[b] **Platinum-based Combination** No regimen proven more effective than another

[c] **Abiraterone contraindications** include hepatic dysfunction, significant cardiovascular disease, uncontrolled hypertension, or the inability to tolerate prednisone

[d] **Docetaxel** prescribe for relatively rapidly progressing symptomatic disease

[e] **Enzalutamide contraindications** include severe renal impairment (CcCl <30 ml/min), seizure history, and/or brain metastases/active epidural disease

[f] **Pembrolizumab** prescribe if patient has MSI-H (microsatellite instability-high), dMMR (deficient mismatch repair) or TMB high in tumor agnostic fashion

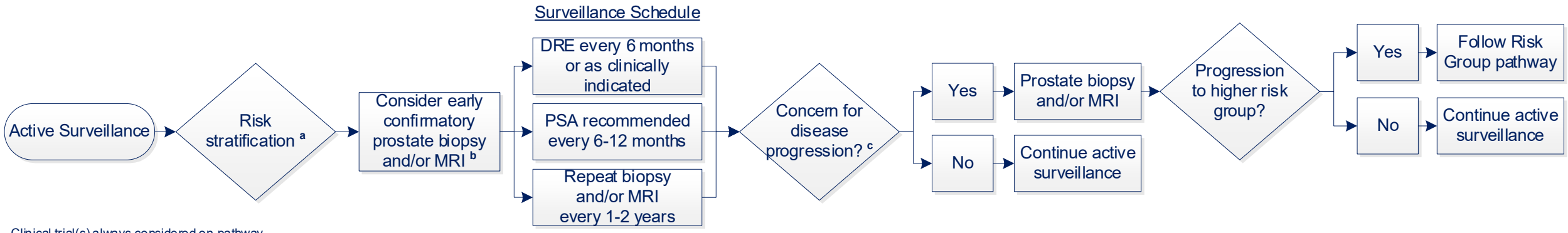
[g] **Cabazitaxel** favored for use after previous failure of one ART (enzalutamide/abiraterone); avoid repeat of previously used therapies

[h] **Radium 223** prescribe if patient has symptomatic bone metastases and no visceral disease

[i] **Olaparib** prescribe if patient has HRRm (Homologous Recombination Repair mutation)

[j] **Contraindications** cannot be given with radium 223, cabazitaxel, or investigational product; patient can continue standard care i.e., AR-directed therapy

Prostate Cancer – Active Surveillance



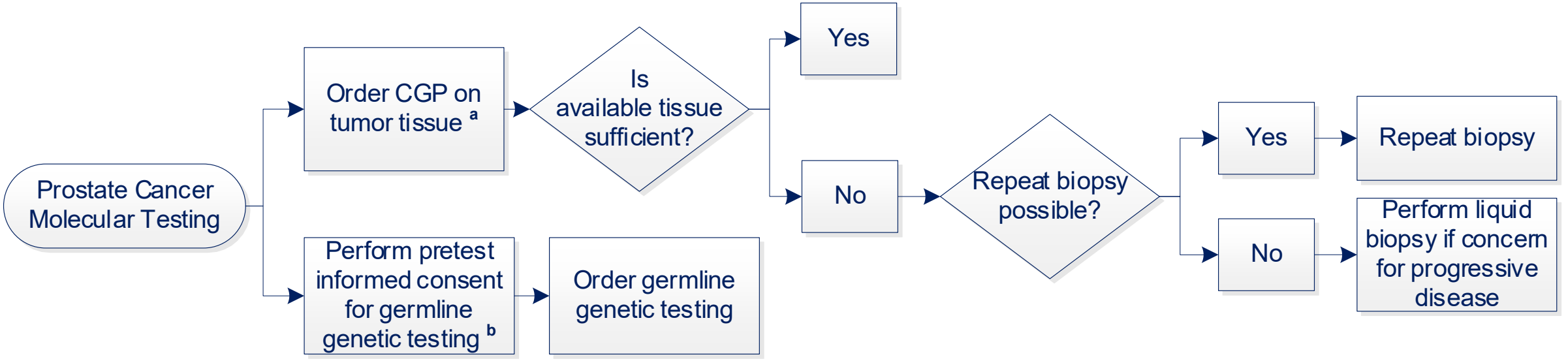
Clinical trial(s) always considered on pathway.

[a] **Risk Stratification** based on a combination of factors that would impact the likelihood of clinically relevant disease progression including: life expectancy (reassess every 1-2 years; if limited life expectancy consider observation), risk group, PSA velocity, DRE, MRI findings, clinical concordance, and patient preference

[b] **Confirmatory prostate biopsy** consider if there is a discordance between pathologic and clinical findings or if initial biopsy is determined to be inadequate

[c] **Concern for disease progression** based on DRE, PSA, and/or MRI results

Prostate Cancer – Molecular Testing



[a] **Comprehensive Genomic Profile (CGP)** for metastatic disease

[b] **Germline Testing** for high risk, very high risk, regional risk, and metastatic disease

Questions?

Contact VHAOncologyPathways@va.gov